IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of: Adair et al.	**Confirmation No. 9631**
Serial No.: 08/846,658	**Art Unit No.: 1642**
Filing Date: May 1, 1997	**Examiner: Minh Tam B. Davis**
For: HUMANISED ANTIBODIES	
Customer No.: 34132	**Docket No.: CARP0001-100**

Filed Via EFS Web
DATE Filed: October 10, 2008

MAIL STOP APPEAL BRIEF- PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

COMMUNICATION

This paper is being filed to inform the Board of a recent Federal Circuit decision and a district court order that Appellants believe are highly relevant to this appeal. In the Examiner's Answer which was filed in this case, the Office equated the determination of whether or not U.S. Patent No. 5,585,089 ("the '089 Queen patent") is entitled to priority as a reference under 35 USC 102(e) with a determination of whether or not the '089 Queen patent is valid and stated that such is not an issue for the Examiner to decide (see page 13 of the Examiner's Answer). As the Federal Circuit recently clarified, however, the presumption of validity is not the equivalent of the presumption of priority. When there is a continuation-in-part application in the chain of priority, the patent is not entitled to a presumption of priority *unless* a priority determination had been made by the Patent Office. See *PowerOasis Inc. v. T-Mobile USA Inc.*, 522 F.3d 1299, 1305, 86 USPQ2d 1385, 1389 (Fed. Cir. 2008) (finding that, when neither the PTO nor the

Board had previously considered priority, "there is simply no reason to presume that claims in a CIP application are entitled to the effective filing date of an earlier filed application"). There are two continuation-in-part applications in the priority chain for the '089 Queen patent. Since there is no presumption of priority, the Board should not maintain this rejection unless a determination of priority had been made previously by the PTO or the Board. Upon review, the undersigned did not find a determination of priority of the claims that issued in the '089 Queen patent during its prosecution. Nor does it appear that any interference has been declared concerning the '089 Queen patent, per the Interference Web Portal.

Appellants maintain this position notwithstanding the Board's recent decision in *Ex Parte Yamaguchi,* Appeal 2007-4412, August 29, 2008. In *Yamaguchi*, the Board effectively overruled a case that has been repeatedly relied upon by Appellants in arguing that the '089 Queen patent is not entitled to its earliest priority dates as a reference under 35 USC 102(e), i.e., *In re Wertheim,* 646 F.2d 527, 209 USPQ 554 (CCPA 1981). *Yamaguchi*, however, does not affect the current appeal. The present facts are similar to those acknowledged by the Board in *Yamaguchi* to still be appropriate for application of the test of *In re Wertheim* – i.e., there are continuation-in-part applications ("cips") in the priority chain.

> **Apart from the narrow fact pattern addressed in Wertheim**, Wertheim's "secret prior art" rationale is inapplicable to determining whether the critical reference date of a U.S. patent or U.S. application publication is the filing date of its underlying provisional application under the statutory scheme of Title 35 as it exists today.

Yamaguchi, p. 12. In footnote 8, *Yamaguchi*, recites the facts in *Wertheim*, i.e., that there were two continuation-in-part applications in the priority chain. In the text citing footnote 8,

Yamaguchi states that, significantly, the two cips added new matter and notes that the court in *Wertheim* observed that, if the new matter was "critical to the patentability of the claimed invention," a patent could not have issued on the earlier filed invention, the theory of patent office delay is not relevant. *Yamaguchi*, paragraph bridging pp. 9-10.

Regardless, even if *Yamaguchi* is applied (even though it should not be), Appellants maintain that the '089 Queen patent is still not an appropriate reference under 35 USC 102(e). Appellants' claims recite the phrase "outside the Kabat and Chothia CDRs." Appellants have repeatedly argued that this phrase is not supported by the two earliest priority documents in the '089 Queen patent priority chain and the Office has failed to point to any support.

In a strained attempt to counter Appellants' argument that the '089 Queen patent is not entitled to its earliest priority date as a reference under 35 USC § 102(e) for the phrase "outside the Kabat and Chothia CDRs," the Office has argued that the unmodified phrase "CDR" in the '089 Queen patent claims should be interpreted to mean "Kabat **or** Chothia" CDR. (S*ee* the Final Rejection dated as mailed July 12, 2004, page 4 and the Office Action dated as mailed May 2, 2005, pages 14-15, emphasis added.) The United States District Court for the District of Delaware ("District Court of Delaware"), however, disagrees.

In a litigation involving patents related to the '089 Queen patent, the Delaware District Court recently ordered that the unmodified phrase "complementary determining region" or "CDR" in the claims of those patents means an "amino acid sequence in the variable region, the boundaries of which are defined by the **Kabat** methodology." (See page 1 of the Order, emphasis added.) The Order and accompanying Memorandum Opinion are enclosed for the Board's convenience. Notably, the interpretation adopted by the Delaware District Court was

the one at asserted by the **plaintiff** (see page 11 of the Memorandum Opinion). The plaintiff is the assignee of the '089 Queen patent.

In view of the foregoing, Appellants respectfully submit that the rejection over the '089 Queen patent should not be maintained and request that the Office withdraw the rejection and declare the interference.

Appellants do not believe that any fee is due. If the event this belief is incorrect, please charge any such fee to Deposit Account 50-3111.

Appellants also note that it has been almost two years since their Reply Brief was filed, or January 22, 2007. Notably, it took the examiner over one year to even acknowledge that the Reply Brief had been filed, or May 6, 2008. This acknowledgement came almost five months after Appellants had filed a status inquiry on January 28, 2008. Per PAIR, the appeal has not even been docketed.

Appellants did not request oral argument in an attempt to move this application forward more expeditiously. It appears that Appellants might have fared better had they requested oral argument. In another matter, in which oral argument was requested, Appellants filed a reply brief on July 3, 2007. The reply brief was acknowledged on August 29, 2007. The appeal was docketed on November 11, 2007, and the hearing was scheduled for April 17, 2008. A decision was handed down May 27, 2008. Thus, although the current rules discourage requesting an oral

argument, and suggest that applications will be handled the same, such does not appear to be the case.

Respectfully submitted,

/Doreen Yatko Trujillo/

Date: October 10, 2008

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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PDL BIOPHARMA, INC.,	:	
	:	
Plaintiff,	:	
	:	
v.	:	Civil Action No. 07-156-JJF
	:	
ALEXION PHARMACEUTICALS, INC.,	:	
	:	
Defendant.	:	

O R D E R

At Wilmington, this 29 day of July 2008, for the reasons discussed in the Memorandum Opinion issued this date;

IT IS HEREBY ORDERED that the following terms and/or phrases in U.S. Patent Nos. 5,693,761 ("the '761 patent"), 5,693,762 ("the '762 patent") and 6,180,370 ("the '370 patent") are assigned the following meanings:

1. The term ""**humanized immunoglobulin**" means an "immunoglobulin comprising a human framework region and one or more CDR's from a non-human (usually a mouse or rat) immunoglobulin." Framework amino acid substitutions are optional.

2. The terms "**complementary determining region**," or "**CDR**," means "amino acid sequence in the variable region, the boundaries of which are defined by the Kabat methodology."

3. The terms "**framework," "framework region"** and **"variable framework regions"** mean "those portions of the variable region of an immunoglobulin that are not a CDR (where the term 'CDR' means 'amino acid sequence in the variable region, the

boundaries of which are defined by the Kabat methodology')."

4. The terms **"heavy and light chain variable region frameworks"** and **"heavy and light chain frameworks"** mean "those portions of the heavy chain and light chain variable regions of an immunoglobulin that are not a CDR (where 'CDR' means 'amino acid sequence in the variable region, the boundaries of which are defined by the Kabat methodology')."

5. The term **"donor immunoglobulin"** is construed to mean "the non-human immunoglobulin providing the CDRs." Framework amino acid substitutions are optional.

6. The terms **"human acceptor immunoglobulin"** and **"acceptor human immunoglobulin"** mean "the human immunoglobulin providing the framework for the CDRs." Framework amino acid substitutions are optional.

7. The term **"humanized immunoglobulin light chain variable region framework"** means "the light chain variable region framework (defined as 'portions of the [light] chain variable region of an immunoglobulin that are not a CDR (where the term 'CDR' means 'amino acid sequence in the variable region, the boundaries of which are defined by the Kabat methodology') of a humanized immunoglobulin (defined as 'an immunoglobulin comprising a human framework region and one or more CDR's from a non-human (usually a mouse or rat) immunoglobulin)'."

8. The term **"humanized immunoglobulin heavy chain variable region framework"** means "the heavy chain variable region

framework (defined as 'portions of the [heavy] chain variable region of an immunoglobulin that are not a CDR (where the term 'CDR' means 'amino acid sequence in the variable region, the boundaries of which are defined by the Kabat methodology')of a humanized immunoglobulin (defined as 'an immunoglobulin comprising a human framework region and one or more CDR's from a non-human (usually a mouse or rat) immunoglobulin)'."

9. The phrases **"DNA segment encoding a humanized heavy chain variable region"/"DNA segment encoding the humanized immunoglobulin heavy chain variable region"** mean "the polynucleotide segment which codes for the humanized heavy chain variable region (as defined above). The segment may either be joined or separate from the segment encoding the light chain."

10. The phrases **"DNA segment encoding a humanized light chain variable region"/"DNA segment encoding the humanized immunoglobulin light chain variable region"** mean "the polynucleotide segment which codes for the humanized light chain variable region (as defined above). The segment may either be joined or separate from the segment encoding the heavy chain."

11. The phrase **"DNA segments encoding the humanized heavy and light chains"** means "the polynucleotide segments which code for the humanized light and heavy chains (as defined above). The segments may be either joined or separate."

12. The phrases **"DNA segments encoding humanized light and heavy chain variable regions"/"DNA segments encoding heavy**

and light chain variable regions of a humanized immunoglobulin" mean "the polynucleotide segments which code for the humanized light and heavy chains (as defined above). The segments may be either joined or separate."

13. The phrase "**synthesizing a [the] DNA segment encoding a humanized heavy chain variable region**" means "producing a [the] polynucleotide segment that codes for the humanized heavy [light] chain variable region (as defined above)."

14. The phrase "**is at least 65% identical**" is construed according to its plain meaning when read in the context of the claim, and further construction by the Court is not required.

Joseph J. Farnan, Jr.
UNITED STATES DISTRICT JUDGE

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

PDL BIOPHARMA, INC.,	:	
	:	
Plaintiff,	:	
	:	
v.	:	Civil Action No. 07-156-JJF
	:	
ALEXION PHARMACEUTICALS, INC.,	:	
	:	
Defendant.	:	

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MEMORANDUM OPINION

July 29, 2008
Wilmington, Delaware.

Farnan, District Judge.

This action was filed by Plaintiff PDL Biopharma, Inc. ("PDL") against Defendant Alexion Pharmaceuticals, Inc. ("Alexion") alleging infringement of U.S. Patent Nos. 5,693,761 ("the '761 patent"), 5,693,762 ("the '762 patent") and 6,180,370 ("the '370 patent") on March 16, 2007. The issue currently before the Court is the claim construction of terms and/or phrases from the patents-in-suit. The parties have briefed their respective positions on claim construction, and the Court has conducted a Markman hearing. This Memorandum Opinion provides the Court's construction of the disputed claim terms and/or phrases.

I. BACKGROUND

The three patents-in-suit share a common specification and are directed to antibody humanization technology and humanized antibodies. Antibodies, also referred to as immunoglobulins, are Y-shaped proteins used by the immune system to identify and neutralize foreign substances called "antigens." Antibodies are composed of four chains: two heavy chains on the interior and two light chains on the exterior. Both the heavy and light chains have two domains, a variable domain, which contains amino acid sequences that vary both within and across immunoglobulin classes, and a constant domain, which contains amino acid sequences that are constant within a class of immunoglobulins.

Within each variable domain, there are three regions called "complementarity determining regions," or "CDRs", the parts of the antibody that recognize and bond to the antigen. The remaining sections of the variable region are called the "framework," which supports the CDR in the proper position within the antibody. PDL's invention relates to "novel methods for preparing humanized immunoglobulin chains," which have generally one or more CDRs from a donor immunoglobulin and a framework region from a human immunoglobulin. '761 patent, Col. 2:37-41.

II. LEGAL STANDARD

Claim construction is a question of law. Markman v. Westview Instruments, Inc., 52 F.3d 967, 977-78 (Fed. Cir. 1995), aff'd, 517 U.S. 370, 388-90 (1996). When construing the claims of a patent, a court considers the literal language of the claim, the patent specification and the prosecution history. Markman, 52 F.3d at 979. Of these sources, the specification is "always highly relevant to the claim construction analysis. Usually it is dispositive; it is the single best guide to the meaning of a disputed term." Phillips v. AWH Corporation, 415 F.3d 1303, 1312-1317 (Fed. Cir. 2005)(quoting Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996). However, "[e]ven when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear

intention to limit the claim scope using 'words or expressions of manifest exclusion or restriction.'" Liebel-Flarsheim Co. v. Medrad, Inc., 358 F.3d 898, 906 (Fed. Cir. 2004)(quoting Teleflex, Inc. v. Ficosa N. Am. Corp., 299 F.3d 1313, 1327 (Fed. Cir. 2002).

A court may consider extrinsic evidence, including expert and inventor testimony, dictionaries, and learned treatises, in order to assist it in understanding the underlying technology, the meaning of terms to one skilled in the art and how the invention works. Phillips, 415 F.3d at 318-319; Markman, 52 F.3d at 979-80 (citations omitted). However, extrinsic evidence is considered less reliable and less useful in claim construction than the patent and its prosecution history. Phillips, 415 F.3d at 318-319 (discussing "flaws" inherent in extrinsic evidence and noting that extrinsic evidence "is unlikely to result in a reliable interpretation of a patent claim scope unless considered in the context of intrinsic evidence").

In addition to these fundamental claim construction principles, a court should also interpret the language in a claim by applying the ordinary and accustomed meaning of the words in the claim. Envirotech Corp. v. Al George, Inc., 730 F.2d 753, 759 (Fed. Cir. 1984). If the patent inventor clearly supplies a different meaning, however, then the claim should be interpreted according to the meaning supplied by the inventor. Markman, 52

F.3d at 980 (noting that patentee is free to be his own lexicographer, but emphasizing that any special definitions given to words must be clearly set forth in patent). If possible, claims should be construed to uphold validity. In re Yamamoto, 740 F.2d 1569, 1571 (Fed. Cir. 1984) (citations omitted).

III. CONSTRUCTION OF THE DISPUTED TERMS AND/OR PHRASES

Two primary disagreements drive the dispute between the parties regarding the scope of PDL's invention: the proper construction of the claim terms "humanized immunoglobulin" and "CDRs." The following asserted claim from the '761 patent is illustrative of how these two terms are used in the asserted claims:

> 1. First and second polynucleotides respectively encoding heavy and light chain variable regions of a humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from human acceptor immunoglobulin heavy and light chain frameworks, which humanized immunoglobulin specifically binds to an antigen with an affinity constant of at least about 10.sup.8 M.sup.-1 and no greater than about four-fold that of the donor immunoglobulin, wherein the sequence of the humanized immunoglobulin heavy chain variable region framework is at least 65% identical to the sequence of the donor immunoglobulin heavy chain variable region framework and comprises at least 70 amino acid residues identical to those in the acceptor human immunoglobulin heavy chain variable region framework.

A. "Humanized Immunoglobulin"

The parties' proposed constructions of the claim term "humanized immunoglobulin" are as follows:

PDL's Construction	Alexion's Construction
"An immunoglobulin comprising a human framework region and one or more CDR's from a non-human (usually a mouse or rat) immunoglobulin." Framework amino acid substitutions are optional.	An immunoglobulin comprising: a human acceptor framework in which one or more amino acids have been replaced by the corresponding amino acid(s) of the donor immunoglobulin; and one or more CDRs from the donor immunoglobulin

In support of its proposed constructions, PDL argues that the specification defines many of the claim terms, including "humanized immunoglobulin," pointing to a column of the patent that begins, "[i]n order that the invention may be more completely understood, several definitions are set forth." '761 Patent, Col. 11:4-5. The specification states: "[a]s used herein, the term 'humanized' immunoglobulin refers to an immunoglobulin comprising a human framework region and one or more CDR's from a non-human (usually a mouse or rat) immunoglobulin." Id. at Col. 12:1-4. Because the specification defines this claim term, PDL contends that the inventor's lexicography governs, and that the Court should construe the term accordingly. PDL further contends that the asserted claims do not require framework amino acid substitutions, as Alexion argues, and that Alexion should not be permitted to improperly import limitations into the claims. PDL contends that its construction is supported by the claim language, since the asserted claims do not, on their face, require framework amino

acid substitutions, and, by contrast, a number of other claims not asserted by PDL, do require them. Accordingly, PDL contends, one of ordinary skill in the art would have concluded that when claims require framework amino acid substitutions, "they say so - and when they do not, they do not." (D.I. 132 at 13.)

PDL further argues that the specification makes clear that framework substitutions are not required by describing framework amino acid substitutions as "possible," "optional," and "another embodiment of the invention," and those claims that reflect this embodiment are not asserted against Alexion. (D.I. 121 at 6.) PDL contends that Alexion cannot rely upon the prosecution history disclaimer law for two reasons: first, because of the PTO's statement regarding the '762 patent application that the "claims are in condition for allowance" based on PDL's explanation that the claims did not require framework amino acid substitutions; (Id. at 8) and second, because the "snippets" from the prosecution history cited by Alexion do not represent a "clear disavowal" of the claims' scope (Id. at 9).

Alexion contends that the Court should construe the phrase "humanized immunoglobulin" to mean "an immunoglobulin comprising: a human acceptor framework in which one or more amino acids have been replaced by the corresponding amino acid(s) of the donor immunoglobulin; and one or more CDRs from the donor immunoglobulin." Alexion contends that the definition in the

specification is not dispositive in this instance because case law holds that the full disclosure of the specification may narrow definitions set forth in the specification where, as here, the proper construction is one that "not only embraces the generalized definition of the term set forth in the specification, but also embraces the feature that PDL continuously emphasized as ***essential*** to its invention: framework substitution." (D.I. 119 at 14.) Alexion contends that the first method described in the invention, creation of a humanized antibody with high affinity by starting with human and mouse sequences with high homology in the framework regions, was known in the art at the time of PDL's filing of its patent application, and accordingly the second method claimed in PDL's patents, framework substitution of amino acids in the human framework region, was the actual crux of PDL's purported invention. (D.I. 96 at 23-24.) Alexion further contends that the examples of the specification support its construction because "each functional humanized immunoglobulin produced had, at a minimum, four framework substitutions," (Id. at 24) and that the patent teaches, and PDL represented to the Patent Trademark Office ("PTO"), that framework substitutions are essential to maintain binding affinity of the mouse antibody. Finally, Alexion contends that one of skill in the art would have understood that the only possible contribution of PDL to the field of antibody

humanization, beyond what was known in the art, was the introduction of framework substitutions outside of the CDRs.

The Federal Circuit has "repeatedly encouraged claim drafters who choose to act as their own lexicographers to clearly define terms used in the claims in the specification." Sinorgchem Co., Shandong v. International Trade Com'n., 511 F.3d 1132, 1136 (Fed. Cir. 2007) (citing, e.g., CCS Fitness, Inc. v. Brunswick Corp., 288 F.3d 1359, 1366 (Fed.Cir. 2002) ("[A] claim term will not receive its ordinary meaning if the patentee acted as his own lexicographer and clearly set forth a definition of the disputed claim term in ... the specification...."); Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed.Cir. 1996) ("The specification acts as a dictionary when it expressly defines terms used in the claims or when it defines terms by implication."). "When the specification explains and defines a term used in the claims, without ambiguity or incompleteness, there is no need to search further for the meaning of the term." Id. at 1138 (citing Multiform Desiccants, Inc. v. Medzam, Ltd., 133 F.3d 1473, 1478 (Fed. Cir. 1998).

The specification states, "[i]n order that the invention may be more completely understood, several definitions are set forth," and then expressly defines "humanized immunoglobulin" as PDL contends, to mean "an immunoglobulin comprising a human framework region and one or more CDR's from a non-human (usually

a mouse or rat) immunoglobulin." '761 Patent, Col. 11:4-5; Id. at Col. 12:1-4. The Court further considers that, within the patents' Abstract and Summary of the Invention, framework amino acid substitutions are described as "possible," "optional," and "another embodiment" of the invention. See '761 Patent, Abstract ("[n]ovel methods for producing, and compositions of, humanized immunoglobulins having one or more complementary determining regions (CDR's) and **possible** additional amino acids from a donor immunoglobulin and a framework region from an accepting human immunoglobulin are provided.")(emphasis added); '761 Patent Col. 2:66-3:7 (describing framework amino acid substitutions as "another embodiment of the present invention" that can be done "separately" or "in conjunction" with the first embodiment).

Accordingly, in light of the express definition provided by the inventor in the specification, the Court will construe the phrase "humanized immunoglobulin" as "an immunoglobulin comprising a human framework region and one or more CDR's from a non-human (usually a mouse or rat) immunoglobulin." Framework amino acid substitutions are optional.

B. "Complementary Determining Region (CDR)"

The parties dispute over the phrase "complementary determining region," or "CDR," centers on whether the boundaries of the amino acid sequence in the variable region are delineated

by the amino acid numbering methodology established by Kabat,[1] as PDL contends, or as delineated by the aggregate of the Kabat methodology and the Chothia[2] methodology, as Alexion contends. The parties' proposed constructions are as follows:

PDL's Construction	Alexion's Construction
Amino acid sequence in the variable region, the boundaries of which are defined by the Kabat methodology	Hypervariable region defined by Kabat together with a hypervariable region as defined by Chothia.

In support of its proposed construction, PDL argues, as above, that the specification explicitly defines the claim term within that portion of the specification that begins, "[i]n order that the invention may be more completely understood, several definitions are set forth." '761 Patent, Col. 11:4-5. The specification then states: "An immunoglobulin light or heavy chain variable region consists of a 'framework' region interrupted by three hypervariable regions, also called CDR's. The extent of the framework region and CDR's have been precisely defined (see, "Sequences of Proteins of Immunological Interest," E. Kabat et al., U.S. Department of Health and Human Services, (1983); which is incorporated herein by reference." '761 Patent,

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[1]See Elvin A. Kabat et al., Sequences of Proteins of Immunological Interest, U.S. Dept. Of Health and Human Services, Public Health Services, National Institutes of Health (1983).

[2]See Cyrus Chothia & Arthur M. Lesk, Canonical Structures for the Hypervariable Regions of Immunoglobulins, 196 J. Mol. Biol. 901 (1987). (D.I. 95 at Exh. 11.)

Col. 11:38-44. PDL contends that the "'drafter clearly, deliberately and precisely defined the term,'" and accordingly, "that precise definition governs." (D.I. 132 at 26, quoting Sinorgchem, 511 F.3d at 1136.) In support of their construction, PDL points to the patents' discussion of the prior art, which "consistently employs the Kabat methodology, " (Id. at 27), and examples in the specification which, PDL contends, define CDR by the Kabat methodology. PDL contends that Alexion's definition "appears only in one section of the specification, twelve columns after the definitions section begins, in a discussion of one particular embodiment...of claims that are not asserted," and that "because the cited passage does not appear in the discussion of other disclosed embodiments" suggests that Alexion's definition does not apply to all of the claims. (D.I. 121 at 25.) Finally, PDL contends that Alexion's argument that statements from the European Patent Office Opposition Proceedings support Alexion's construction must fail because statements in those European records are legally immaterial, and factually inapposite. (D.I. 121 at 28.)

Alexion contends that the specification of the patent-in-suit sets forth competing definitions of the term "CDR," but ultimately adopts the definition of CDR as that of Kabat together with Chothia, as set forth in Column 23:9-15 of the '761 Patent:

> The chains all exhibit the same general structure of relatively conserved framework regions joined by three

> hypervariable regions, also called Complementarity Determining Regions or CDR's (see 'Sequences of Proteins of Immunological Interest,' Kabat E. Et al., US Department of Health and Human Services (1983); and Chothia and Lesk, J. Mol. Biol., 196, 901-917 (1987), which are incorporated herein by reference.

Alexion contends that, even if PDL's patents did set forth the Kabat definition, PDL disclaimed this construction during prosecution in arguing over the prior art, by limiting "its claimed invention to humanized immunoglobulins containing the specific definition of "CDR" adopted by PDL, *i.e.*, the Kabat CDR plus Chothia CDR H1." (D.I. 86 at 12.) Alexion contends that this disclaimer trumps any contrary definition PDL set forth in the specification. Alexion further contends that, during the prosecution of its related European patents, PDL argued that CDR meant Kabat CDR taken together with the Chothia definition of CDR, and that PDL should not be permitted to reverse its position. Finally, Alexion contends that PDL has admitted in this litigation that CDR means Kabat plus Chothia by an infringement chart provided to Alexion "for purposes of identifying claims that Alexion may wish to construe" on December 28, 2007. (D.I. 119 at 9.) The chart states that Alexion's antibody contains a certain number of amino acids in the framework regions, a figure that includes amino acids that were outside the CDR H1 as defined by both Kabat and Chothia. (Id.)

After reviewing the claim language and the specification, the Court concludes that "CDR" means, as PDL contends, "amino

acid sequence in the variable region, the boundaries of which are defined by the Kabat methodology." As discussed above, the specification contains a "definitions" section which explicitly defines CDR as defined by Kabat, and, "when it expressly defines terms used in the claims," the specification acts as a dictionary. Vitronics Corp., 90 F.3d at 1582. The Court is not persuaded by Alexion's contention that the specification ultimately adopts the definition of CDR as that of Kabat together with Chothia, as set forth in Column 23:9-15 of the '761 Patent, because Alexion offers no plausible explanation as to why the inventor would make the effort to explicitly and clearly define the term "CDR" in the "definitions" section of the patent in Columns 10-11, if he actually intended that CDR be defined as set forth in Column 23. Later references in the specification to Chothia do not alter the explicit definition set forth in the specification's definitions section.

The Court has also considered Alexion's argument regarding the prosecution history of the patents, but concludes that the relevant portions are not sufficient to establish the requisite "clear disavowal of claim scope." NTP, Inc. v. Research In Motion, Ltd., 418 F.3d 1282, 1309 (Fed. Cir. 2005)

C. "Framework" terms

The parties have jointly requested that the Court construe the claim terms "framework," "framework region,"[3] and "variable region frameworks," which are used interchangeably in the claims of the patents-in-suit, to mean "those portions of the variable region of an immunoglobulin that are not a CDR (where the term 'CDR' is used as construed by the Court)." The Court having construed "CDR" as depicted above, the Court construes the claim terms "framework," "framework region," and "variable region frameworks" to mean "those portions of the variable region of an immunoglobulin that are not a CDR (where the term 'CDR' means 'amino acid sequence in the variable region, the boundaries of which are defined by the Kabat methodology')."

The parties have also jointly requested that the Court construe the claim terms "heavy and light chain variable region

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[3] The claim term "framework substitutions" does not appear in the claims PDL has asserted against Alexion. It does, however, appear in the Counterclaims asserted by Alexion against PDL in this litigation. This is true for the term "hypervariable regions," as well. PDL did not provide constructions for either term, arguing that neither term is in controversy.

The Court's understanding, informed by the parties' claim construction briefing, is that PDL has provided Alexion with a proposed unilateral covenant not to sue Alexion regarding certain claims, which, in PDL's view, moots Alexion's counterclaim. (D.I. 119 at 1; D.I. 132 at 1.) Alexion does not agree that PDL's proposed covenant is sufficient to moot its counterclaim. Accordingly, the parties should promptly notify the Court of the status of their negotiations regarding PDL's proposed covenant. If necessary at that juncture, the Court will then construe the claim terms "framework substitutions" and "hypervariable regions."

frameworks" and "heavy and light chain frameworks" as interchangeable terms meaning "those portions of the heavy chain and light chain variable regions of an immunoglobulin that are not a CDR (where the term 'CDR' is used as construed by the Court." Accordingly, the Court construes the claim terms "heavy and light chain variable region frameworks" and "heavy and light chain frameworks" to mean "those portions of the heavy chain and light chain variable regions of an immunoglobulin that are not a CDR (where the term 'CDR' means 'amino acid sequence in the variable region, the boundaries of which are defined by the Kabat methodology')."

D. "Donor Immunoglobulin" and "Human Acceptor Immunoglobulin"

The parties agree that the term "donor immunoglobulin" in the asserted claims is the non-human immunoglobulin providing the CDRs in the acceptor human immunoglobulin/human acceptor immunoglobulin. (D.I. 132 at 20; D.I. 96 at 30.) They further agree that "human acceptor immunoglobulin" and "acceptor human immunoglobulin" are synonymous in the asserted claims, and are the "human immunoglobulin used to form the scaffolding of the humanized antibody," (D.I. 96 at 30) or the framework for the CDRs from the donor immunoglobulin (D.I. 132 at 20). The parties disagree, however, as to whether these terms require "that the non-human donor immunoglobulin provide additional amino acid substitutions that the human acceptor immunoglobulin must

accept." (D.I. 132 at 20.)

PDL argues that the specification expressly defines "donor immunoglobulin" and the "human acceptor immunoglobulin"/"acceptor human immunoglobulin": "As used herein, the term 'humanized' immunoglobulin refers to an immunoglobulin comprising a human framework region and one or more CDR's from a non-human (usually a mouse or rat) immunoglobulin. The non-human immunoglobulin providing the CDR's is called the 'donor' and the human immunoglobulin providing the framework is called the acceptor." '761 Patent Col 12:1-7. PDL contends that nothing in this definition requires framework substitutions, and that the express definition should govern the Court's construction.

Alexion contends that the Court should construe the claim term "donor immunoglobulin" to mean "a non-human immunoglobulin that provides at least one CDR and at least one framework amino acid to a human acceptor immunoglobulin," and the claim terms "human acceptor immunoglobulin" and "acceptor human immunoglobulin" to each mean "a human immunoglobulin that takes at least one CDR and at least one framework amino acid from a donor immunoglobulin." Alexion contends that these constructions recognize "PDL's assertions in the specification and during prosecution that framework substitutions in the human acceptor immunoglobulin are essential to PDL's invention." (D.I. 96 at 31.)

In light of the Court's determination that the claim term "humanized immunoglobulin," as expressly defined in the specification, does not require framework substitutions (see § IV(A) *supra*), the Court will adopt PDL's construction of the disputed terms. Accordingly, "donor immunoglobulin" is construed to mean "the non-human immunoglobulin providing the CDRs." "Human acceptor immunoglobulin" and "acceptor human immunoglobulin" are each construed to mean "the human immunoglobulin providing the framework for the CDRs."

E. "Humanized Immunoglobulin Light Chain Variable Region Framework" and "Humanized Immunoglobulin Heavy Chain Variable Region Framework"

Here again, Alexion argues that the Court should construe the claim terms "humanized immunoglobulin light chain variable region framework" and "humanized immunoglobulin heavy chain variable region framework" to require framework substitutions. The Court having determined that the claim term "humanized immunoglobulin," as expressly defined in the specification, does not require framework substitutions (see § IV(A) *supra*), the Court will adopt PDL's proposed constructions, and will construe "humanized immunoglobulin light chain variable region framework" to mean "the light chain variable region framework (defined as 'portions of the [light] variable region of an immunoglobulin that are not a CDR (where the term 'CDR' means 'amino acid sequence in the variable region, the boundaries of which are

defined by the Kabat methodology") of a humanized immunoglobulin (defined as 'an immunoglobulin comprising a human framework region and one or more CDR's from a non-human (usually a mouse or rat) immunoglobulin')." The Court will construe "humanized immunoglobulin heavy chain variable region framework to mean "the heavy chain variable region framework (defined as 'portions of the [heavy] variable region of an immunoglobulin that are not a CDR (where the term 'CDR' means 'amino acid sequence in the variable region, the boundaries of which are defined by the Kabat methodology") of a humanized immunoglobulin (defined as 'an immunoglobulin comprising a human framework region and one or more CDR's from a non-human (usually a mouse or rat) immunoglobulin')."

F. "DNA Segment Encoding" Terms

The parties dispute the construction of four related claim terms that begin "DNA segment[s] encoding." These terms are:

- "DNA segment encoding a humanized heavy chain variable region"/"DNA segment encoding the humanized immunoglobulin heavy chain variable region";
- "DNA segment encoding a humanized light chain variable region"/"DNA segment encoding the humanized immunoglobulin light chain variable region";
- "DNA segments encoding the humanized heavy and light chains";

- "DNA segments encoding humanized light and heavy chain variable regions"/"DNA segments encoding heavy and light chain variable regions of a humanized immunoglobulin."

First, as above, Alexion contends that the humanized immunoglobulin of PDL's invention requires a framework amino acid substitution. The Court has determined otherwise, as discussed in § IV(A), *supra*. The parties' remaining dispute over these claim terms is whether "DNA segments" means two or more polynucleotides, or "one segment that is joined or two segements that are joined as part of one larger polynucleotide." (D.I. 132 at 33.)

Alexion contends that "DNA segment encoding" means a DNA segment or polynucleotide that codes for the amino acids of the respective protein chains recited in the claim terms. Alexion further contends that the Court should construe "DNA segments encoding" as "two or more polypeptides encoding," since "DNA segments" is a plural claim phrase, and Alexion's construction comports with the specification and the understanding of one of skill in the art. According to Alexion, a single DNA sequence will always code for the same amino acid sequence, thus "'DNA segments encoding' two different amino acid sequences (e.g., a light chain and a heavy chain) necessarily must be at least two different polynucleotides, one coding for each amino acid sequence." (D.I. 119 at 29.)(emphasis removed)

While PDL agrees with Alexion that "encoding" means "that contains the DNA sequence that encodes for," PDL contends that one of ordinary skill in the art at the time would have known that "'DNA segments encoding' meant polynucleotides that encode, whether those were joined on one larger polynucleotide or whether they were separate." (D.I. 132 at 33.) PDL points the Court to extrinsic evidence, and contends that these references confirm that "one of ordinary skill in the art at the time would have known the 'DNA segments encoding' could be one segment that is joined or two segments that are joined as part of one larger polynucleotide." (Id.) PDL contends that its construction is supported by the patents' specification, the prior art incorporated into the patents, and the prosecution history.

PDL further argues that "DNA segment encoding" should not be limited to "a polynucleotide encoding," as Alexion proposes, since PDL contends that one of ordinary skill in the art would have known that "DNA segment encoding" could be one segment that is joined or two segments that are joined as part of one larger polynucleotide.

Having reviewed the parties's construction of the "DNA segment[s] encoding" terms, the Court will adopt PDL's proposed construction, having found nothing in the claim language or specification that indicates that two or more segments may not be part of single, larger polynucleotide, and will construe the

terms as follows:

- "DNA segment encoding a humanized heavy chain variable region"/"DNA segment encoding the humanized immunoglobulin heavy chain variable region" means "the polynucleotide segment which codes for the humanized heavy chain variable region (as defined above). The segment may either be joined or separate from the segment encoding the light chain."
- "DNA segment encoding a humanized light chain variable region"/"DNA segment encoding the humanized immunoglobulin light chain variable region" means "the polynucleotide segment which codes for the humanized light chain variable region (as defined above). The segment may either be joined or separate from the segment encoding the heavy chain."
- "DNA segments encoding the humanized heavy and light chains" means "the polynucleotide segments which code for the humanized light and heavy chains (as defined above). The segments may be either joined or separate."
- "DNA segments encoding humanized light and heavy chain variable regions"/"DNA segments encoding heavy and light chain variable regions of a humanized immunoglobulin" mean "the polynucleotide segments which code for the humanized light and heavy chains (as defined above). The segments may be either joined or separate."

G. "Synthesizing a [the] DNA segment encoding a humanized heavy [light] chain variable region"

The parties dispute the construction of the phrase "synthesizing a [the] DNA segment encoding a humanized heavy chain variable region." The parties proposed constructions are as follows:

PDL's Construction	Alexion's Construction
Producing a [the] polynucleotide segment that codes for the humanized heavy [light] chain variable region (as defined by the Court)	Producing a polynucleotide encoding the entire humanized heavy [light] chain variable region by synthesizing *de novo* and ligating oligonucleotides.

Alexion contends that the patent specification supports its construction because it distinguishes between synthetic production of DNA, and DNA production made by other methods. Alexion contends that the "preferred method of synthesizing and ligating oligonucleotides to produce the DNA segments of the invention is set forth in several examples of the patents-in-suit." (D.I. 96 at 36.) Alexion further contends that one of ordinary skill in the art would have been well versed in methods of synthesizing proteins by creating and ligating oligonucleotides, and despite the fact that such methods were "expensive, time consuming and labor intensive," would have known that such synthesis was necessary for the production of amino acid chains, since "the starting materials for PCR-based methods of making proteins were largely unavailable." (Id. at 37.)

In response, PDL contends that Alexion's definition is circular, ambiguous and cannot be reconciled with the claim

language, the specification, the prior art incorporated into the specification, or the common understanding of one of ordinary skill in the art. PDL points to language in the Summary of the Invention that states "[o]nce designed, the immunoglobulins, including binding fragments and other immunoglobulin forms, of the present invention may be produced readily by a variety of recombinant DNA or other techniques," ('762 Patent, Col. 3:44-47) and to the Detailed Description of the Invention that discloses synthesizing by a variety of techniques. PDL contends that Alexion's construction attempts to impermissibly import a limitation from the specification, and to make the "preferred method" of synthesizing "required." (D.I. 121 at 22.) PDL further contends that one of ordinary skill in the art would have understood that "'synthesizing' is synonymous with 'producing' a polynucleotide and is not limited to 'synthetic production.'" (Id. at 23.)

After reviewing the claim language and the specification, the Court concludes that, in the context of the asserted claims, "synthesizing a [the] DNA segment encoding a humanized heavy chain variable region" means, as PDL contends, "producing a [the] polynucleotide segment that codes for the humanized heavy [light] chain variable region (as defined by the Court)." While the specification of the patent indicates that synthetic production is the preferred production method ('762 Patent, Col. 3:44-50),

Alexion admits that the specification describes other production techniques for the production of polynucleotides. (D.I. 119 at 31.) See, e.g., 762 Patent, Col. 17:50-61, Col. "[C]ase law makes clear that while an accused infringer may overcome the heavy presumption of ordinary meaning and narrow a claim term's ordinary meaning, he cannot do so simply by pointing to the preferred embodiment or other structures or steps disclosed in the specification or prosecution history." SunRace Roots Enterprise Co., Ltd. v. SRAM Corp., 336 F.3d 1298, 1305 (Fed. Cir. 2003). The Court will not limit methods of production to the preferred method in light of the language of the claims and specification indicating that the inventor contemplated that other methods might be used.

F. "Is At Least 65% Identical"

Finally, the parties disagree as to whether the claim term "is at least 65 percent identical" requires construction. PDL contends that Alexion has "suggested that the specified percentage identity be made on the basis of comparisons of nucleotides that code for amino acids, rather than amino acid sequences themselves," and that this suggestion cannot be reconciled with the patents, the claims, or the understanding of one of ordinary skill at the art. By its briefing, however, Alexion contends that this term does not require construction, and that the plain meaning of the term would be clear to one of

skill in art.

The Court agrees with Alexion, and finds that this claim term does not require construction since its plain meaning would be clear to one of skill in the art.

IV. CONCLUSION

For the reasons discussed, the Court has construed the disputed terms and/or phrases of the '761 patent, the '762 patent and the '370 patent as provided herein. An Order consistent with this Memorandum Opinion will be entered setting forth the meaning of the disputed terms and/or phrases in the '761 patent, the '762 patent and the '370 patent.